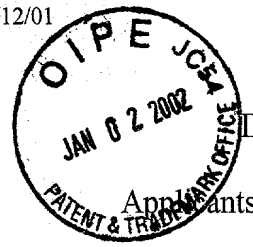
#3

::ODMA\MHODMA\iManage;264374;1
LMT/MMY/kmb
11/12/01

PATENT APPLICATION
Docket No.: 2825.2001-001



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: James C. Engert, Marie-Claude Vohl, Carl Brewer, Kenneth Morgan, Daniel Gaudet and Thomas J. Hudson

Application No.: 09/802,320 Group: 1632

Filed: March 8, 2001 Examiner: Not Assigned

For: Very Low Density Lipoprotein Receptor Polymorphisms and Uses Therefor

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231

on 11-21-01 Denise Caredo
Date Signature

Denise Caredo
Typed or printed name of person signing certificate

TRANSMITTAL OF SEQUENCE LISTING AND PRELIMINARY AMENDMENT IN REPLY TO NOTICE TO FILE MISSING PARTS

Box Sequence

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

This paper is submitted in response to the Notice to File Missing Parts of Application, mailed from the Patent Office on May 23, 2001. A copy of the Notice is attached.

Applicants' Attorney requests an extension of time to respond to the Notice. A Petition for Extension of Time and the appropriate fees are being filed concurrently.

Transmitted herewith is a copy of the "Sequence Listing" (sheets 1/4 through 4/4) in paper form for the above-identified patent application as required by 37 C.F.R. §1.821(c) and a copy of the "Sequence Listing" in computer readable form as required by 37 C.F.R. §1.821(e). As required by 37 C.F.R. §1.821(f), Applicants' Attorney hereby states that the content of the "Sequence Listing" in paper form and the computer readable form of the "Sequence Listing" are the same and, as required by 37 C.F.R. §1.821(g), also states that the submission includes no new matter.

Applicants' Attorney submits the following amendments to comply with 37 C.F.R. §1.825:

In the Specification

Please insert the attached "Sequence Listing" (sheets 1/4 through 4/4), and comprising SEQ ID NOS: 1-22, into the above-referenced application.

Please replace the paragraph at page 5, line 20, with the following:

- - -Figs. 1A and 1B show the results of fine mapping of chromosome 9.- - -

Please replace the paragraph at page 5, lines 21-22, with the following:

- - -Figs. 2A-2D show the results of an association study performed on 204 cases and 117 controls.- - -

Please replace the paragraph at page 32, lines 6-13, with the following:

- - - An initial whole genome scan was performed on 167 individuals from 22 families. This allowed the identification of four chromosomal regions with NPL scores greater than 1.60. One of these peaks (NPL score = 2.35) was at D9S925. Using the GeneMap '98 (http://www.ncbi.nlm.nih.gov/genemap/), it was determined that the VLDLr gene locus was located within 23 cM of D9S925. In subsequent fine mapping of this region with 21 additional families and six additional markers from the region, the peak shifted to D9S285, and the NPL value increased to 2.79. This marker is estimated to be about 20 cM from the VLDLr locus (Figs. 1A and 1B).- - -

Please replace the paragraph at page33, lines 5-12, with the following:

- - - In the Chicoutimi case-control cohort, the major alleles had repeat sizes of 5, 8 and 9, which accounted for 98% of all alleles. Minor alleles with repeat sizes of 7, 10 and 11 were seen in this population. In the association study, performed on 204 cases and 117 controls, it was determined that individuals who are homozygous for five repeats, the "5/5 genotype", have a reduced susceptibility to CHD (odds ratio of 0.55 at the 0.046 significance level) (see Figs. 2A-2D). The case control study also found odds ratios of 1.45 and 1.60 for the 8/8 and the 8/9 genotypes, respectively, but neither of these results was statistically significant.- - -

CONCLUSION

Changes have been made to the specification to reflect the renumbering of the Figures. No new matter has been added. Entry of the Preliminary Amendment is respectfully requested. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Lisa M. Treannie

Lisa M. Treannie
Registration No. 41,368
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133
Date: 11/21/01

MARKED UP VERSION OF AMENDMENTS

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Replace the paragraph at page 5, line 20 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

- - -[Fig. 1] Figs 1A and 1B show the results of fine mapping of chromosome 9. - - -

Replace the paragraph at page 5, lines 21-22, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

- - - [Fig 2] Figs. 2A-2D show the results of an association study performed on 204 cases and 117 controls.- - -

Replace the paragraph at page 32, lines 6-13, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

- - -An initial whole genome scan was performed on 167 individuals from 22 families. This allowed the identification of four chromosomal regions with NPL scores greater than 1.60. One of these peaks (NPL score = 2.35) was at D9S925. Using the GeneMap '98 (http://www.ncbi.nlm.nih.gov/genemap/), it was determined that the VLDLr gene locus was located within 23 cM of D9S925. In subsequent fine mapping of this region with 21 additional families and six additional markers from the region, the peak shifted to D9S285, and the NPL value increased to

2.79. This marker is estimated to be about 20 cM from the VLDLr locus [(Fig.1).] (Figs. 1A and 1B).- - -

Replace the paragraph at page 33, lines 5-12, with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

- - -In the Chicoutimi case-control cohort, the major alleles had repeat sizes of 5, 8 and 9, which accounted for 98% of all alleles. Minor alleles with repeat sizes of 7, 10 and 11 were seen in this population. In the association study, performed on 204 cases and 117 controls, it was determined that individuals who are homozygous for five repeats, the "5/5 genotype", have a reduced susceptibility to CHD (odds ratio of 0.55 at the 0.046 significance level) [(see Fig. 2).] (see Figs. 2A-2D). The case control study also found odds ratios of 1.45 and 1.60 for the 8/8 and the 8/9 genotypes, respectively, but neither of these results was statistically significant.- - -